

Pharmaceutical Residues in the Environment

- Much Ado about Nothing?

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Drug Residues in the Environment - *Much Ado about Nothing?*



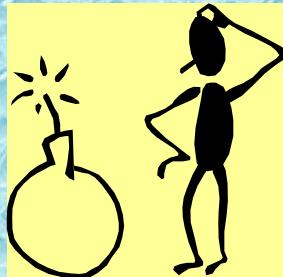
What is the problem?



How do you want to solve the problem?



What will happen, if the problem is not solved?



Metabolism of pharmaceuticals

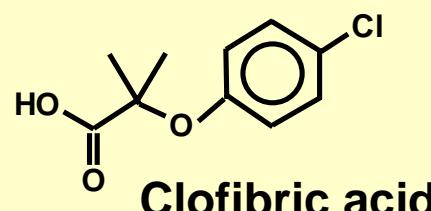
drugs

phase I
oxidation
reduction
hydrolysis

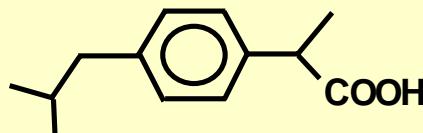
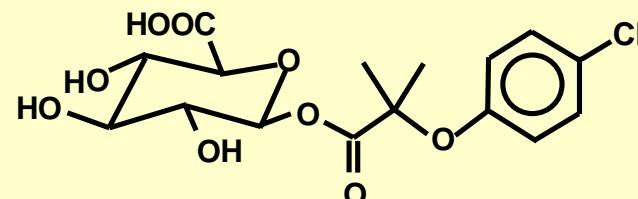
metabolite
phase I

phase II
conjugation
with glucuronic acid
sulphate, amino acid

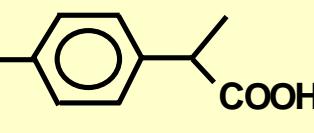
metabolite
phase II



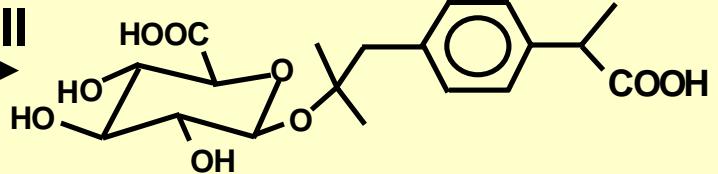
phase II



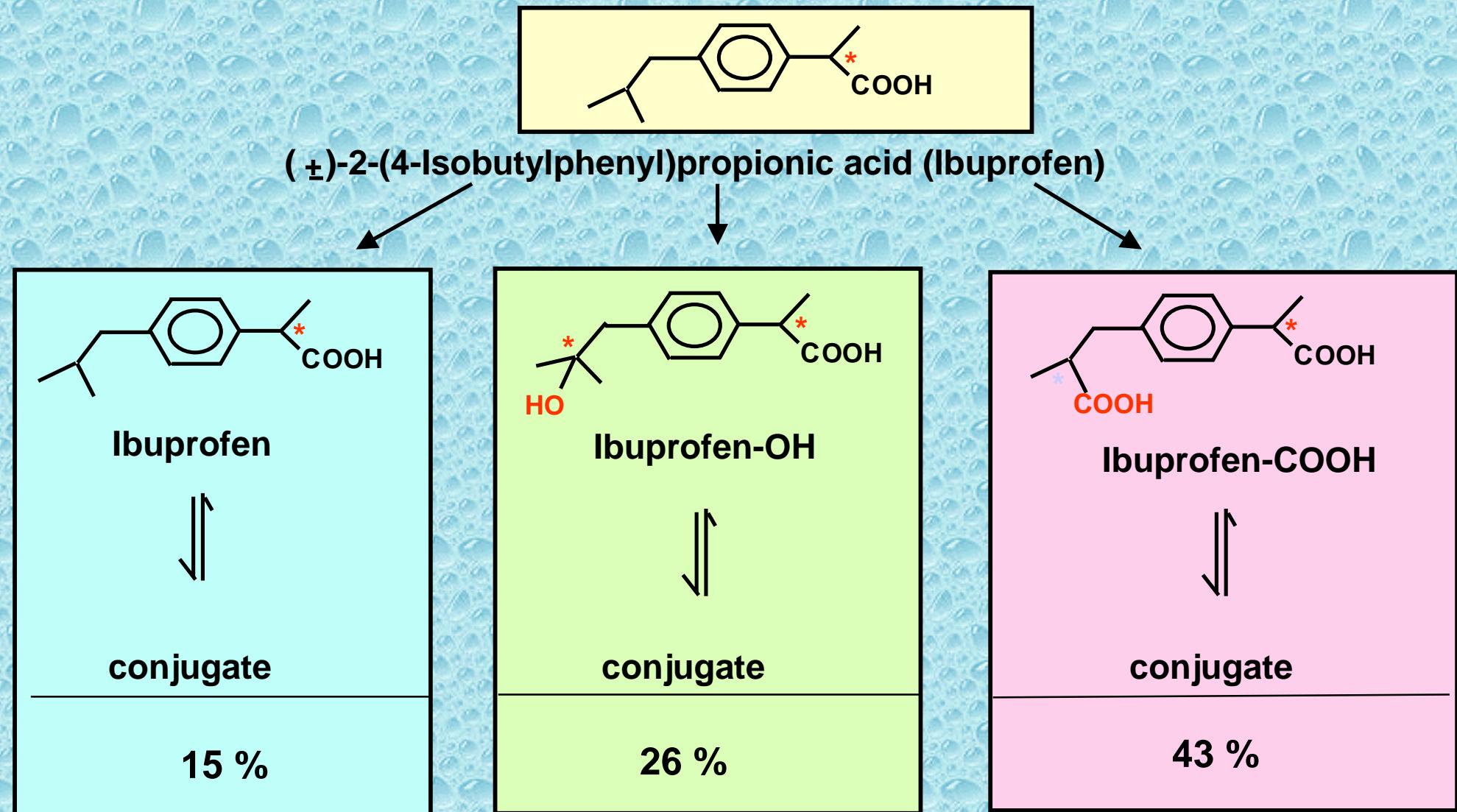
phase I



phase II



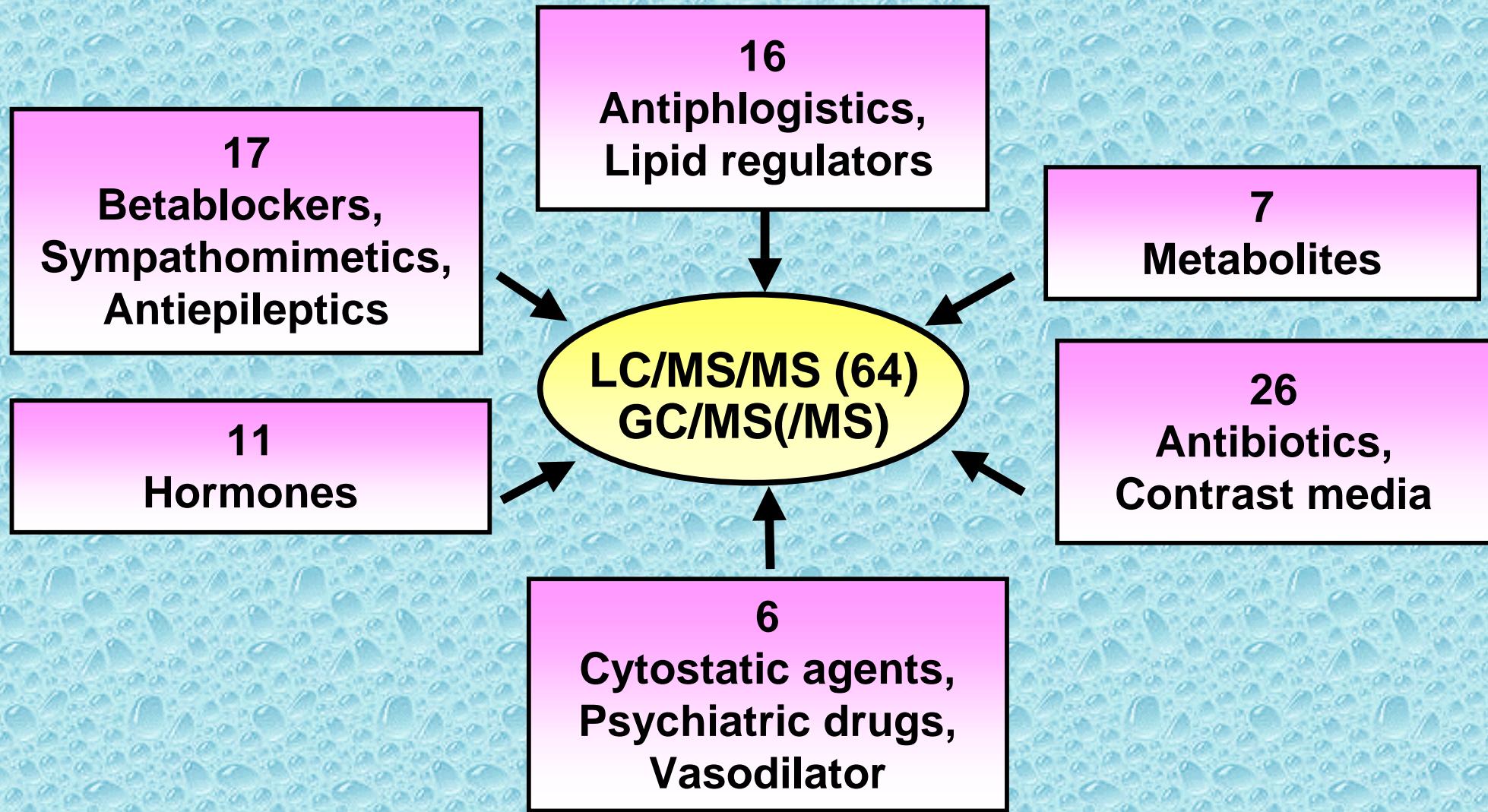
Metabolism and excretion of Ibuprofen



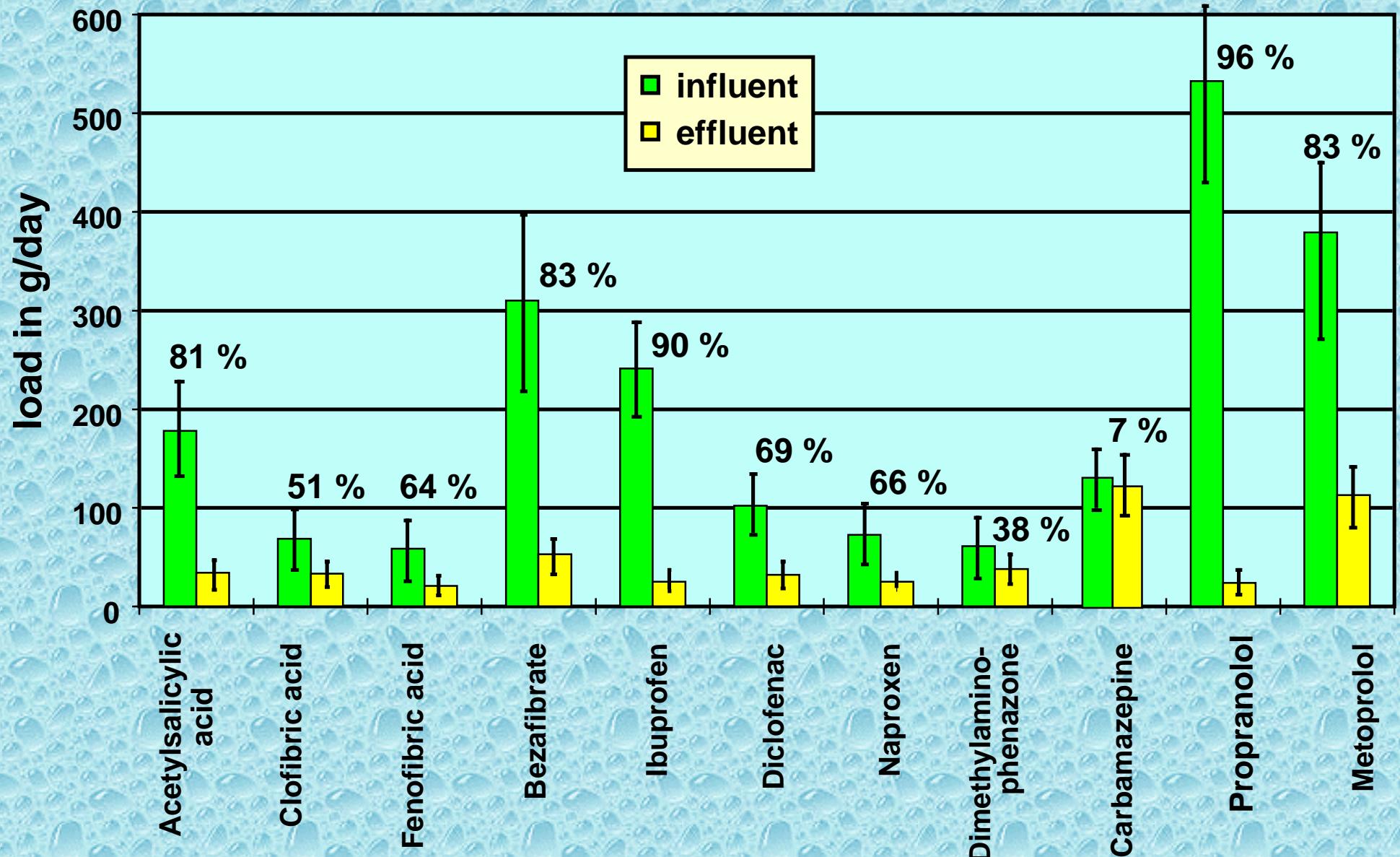
Yearly prescribed amounts in Germany

<i>Pharmaceuticals in human medicine</i>	1997 in tons
Bezafibrate	45
Carbamazepine	80
Metoprolol	52
Sulfamethoxazol	60
Diclofenac	75
Ibuprofen	180
Acetylsalicylic acid	>500
Iopromide	130
17 α -Ethinylestradiol	0.050

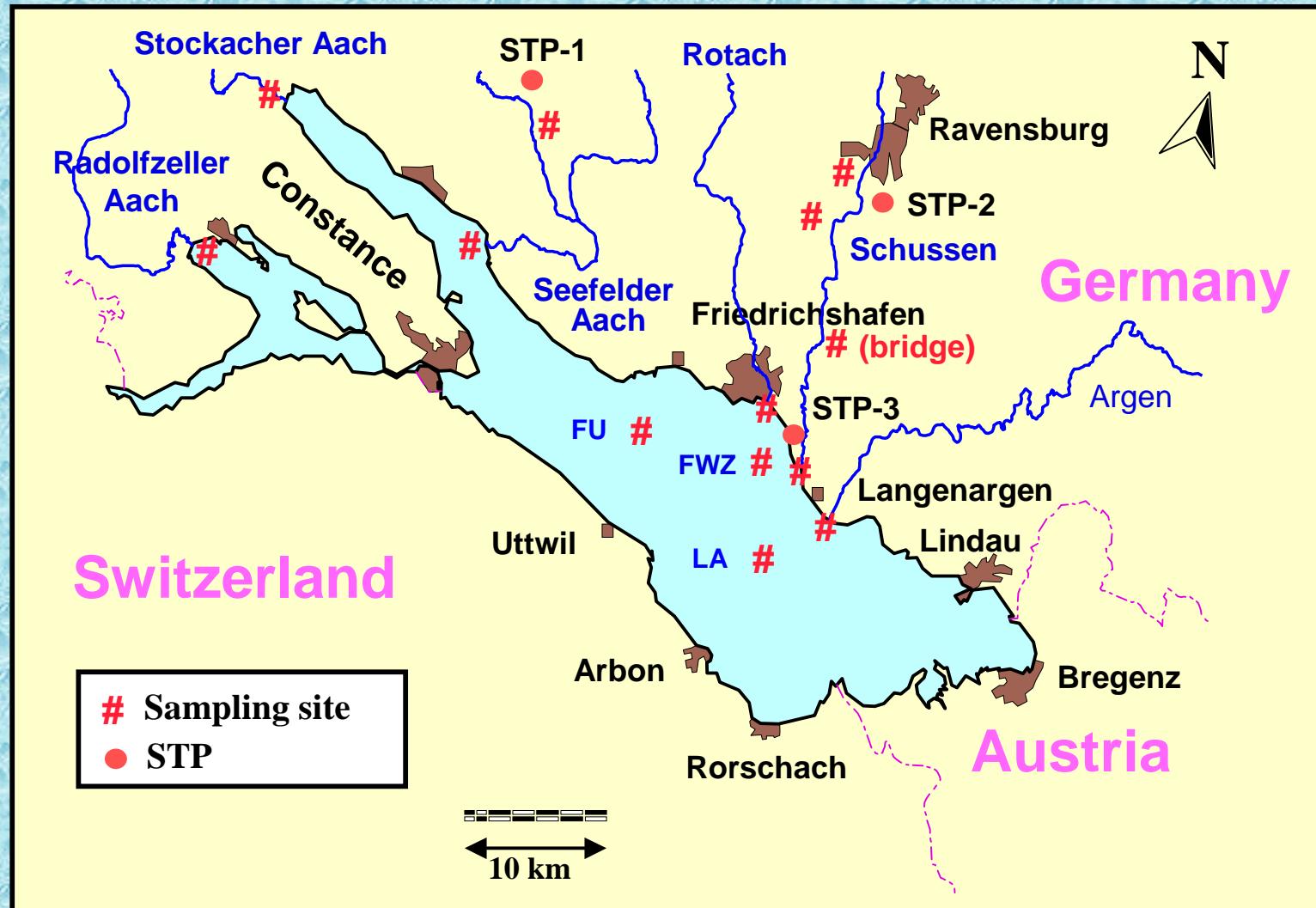
Analytical methods for 83 drugs, hormones and metabolites



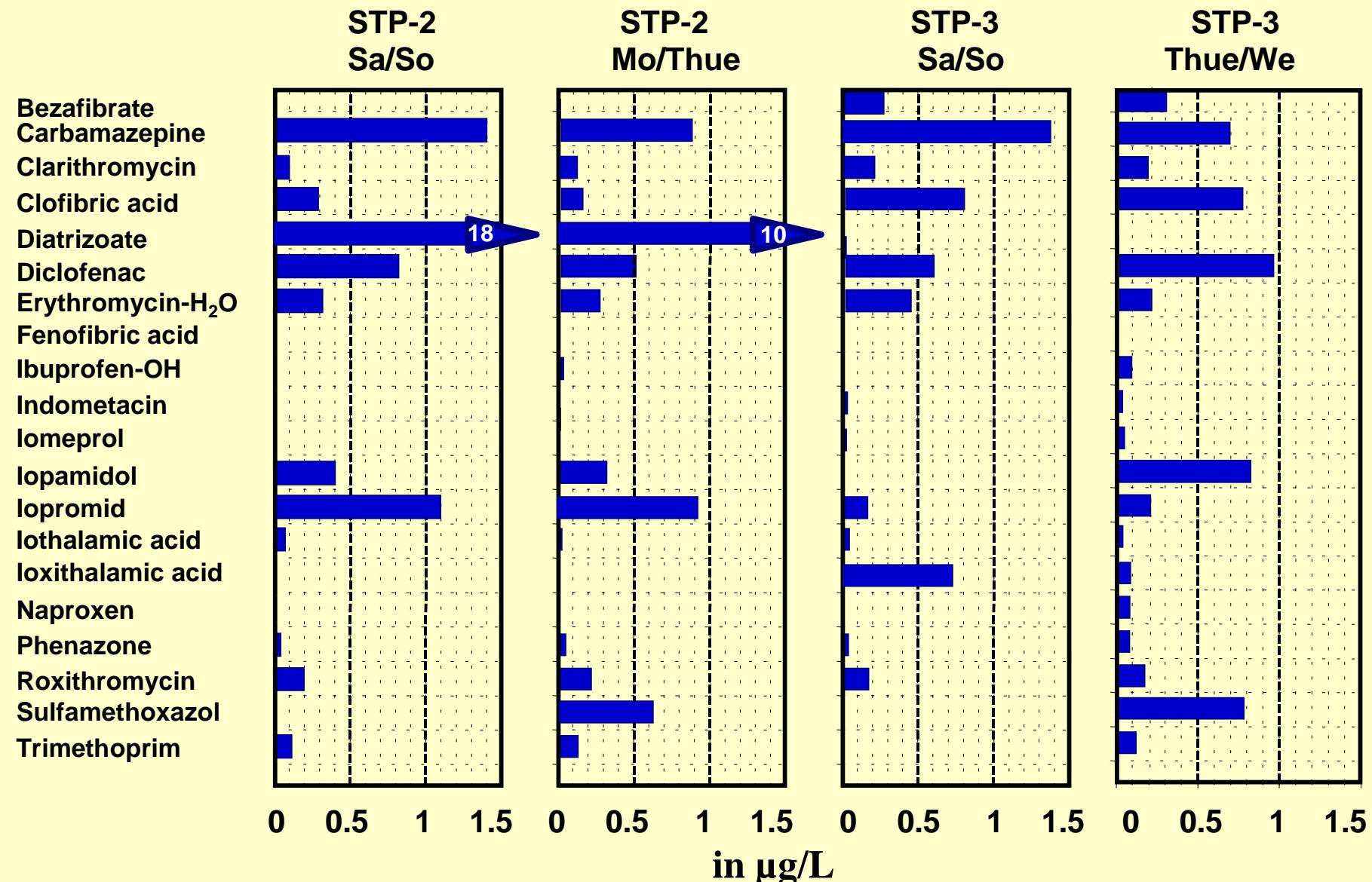
Elimination of acidic drugs in a municipal sewage treatment plant



Lake Constance and its tributaries



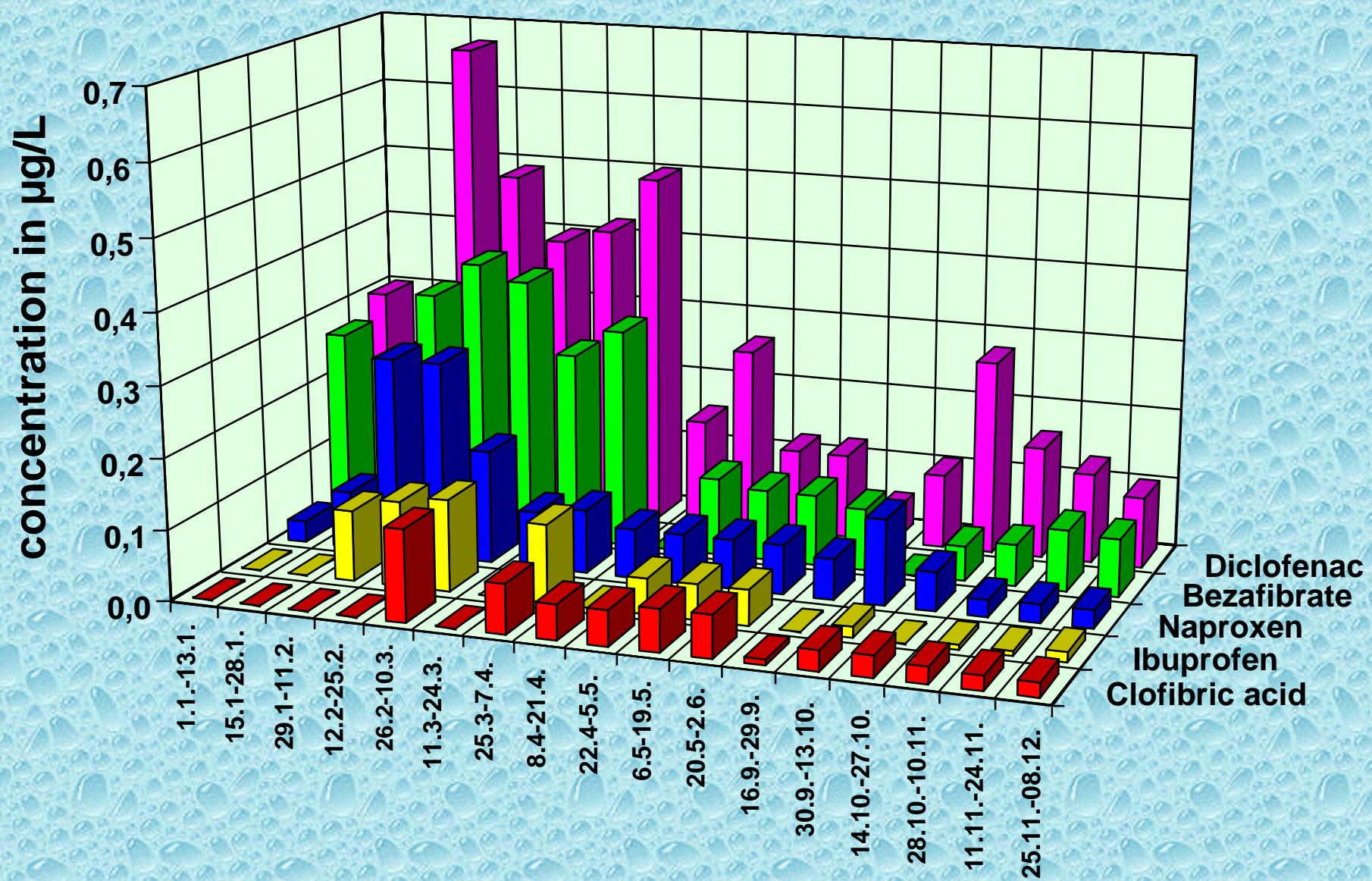
Drugs in daily composite samples of STP effluents



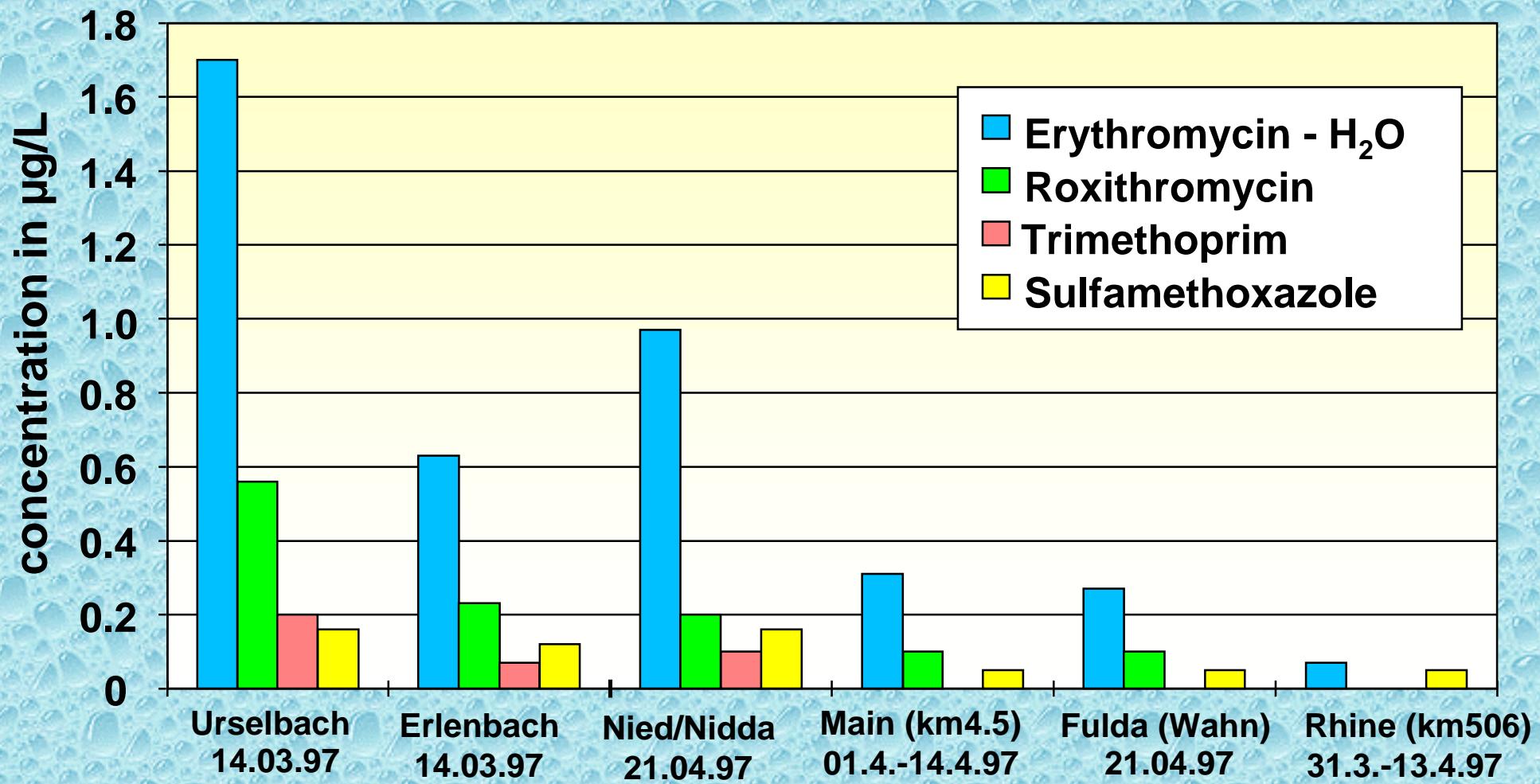
Number of detected drugs in lake Constance and tributaries

	Number of drugs monitored	detected
Analgesics	3	1
Antibiotics	17	6
Antiepileptics	1	1
Antirheumatics	10	6
Betablockers	7	1
Sympathomimetics	4	-
Vasodilators	1	-
Lipid regulator	7	3
Estrogens	5	-
Psychiatric drugs	1	-
Contrast media	6	6
Cytostatic agents	2	-
Sum	64	24

Acidic Drugs in the River Rhine



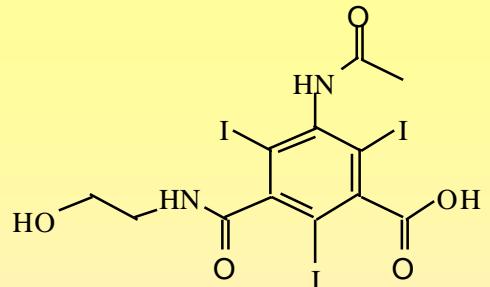
Screening of rivers and creeks



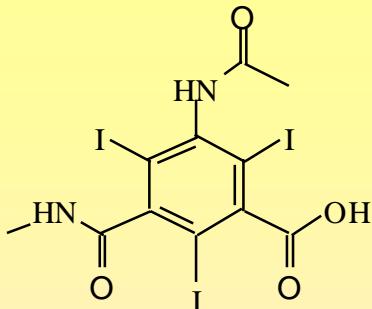
Exposure of STP effluents and rivers with *antibiotics*

substance (conc. in µg/L)	STP effluents median 90-percentile		rivers and creeks median 90-percentile	
Erythromycin-H ₂ O	2.5	5.1	0.15	0.63
Clarithromycin	0.14	0.24	<BG	0.15
Roxithromycin	0.68	0.80	<BG	0.20
Sulfamethoxazole	0.40	0.90	0.03	0.14
Trimethoprim	0.32	0.62	<BG	0.09

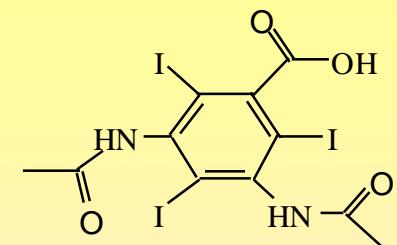
Iodinated contrast media



loxithalamic acid



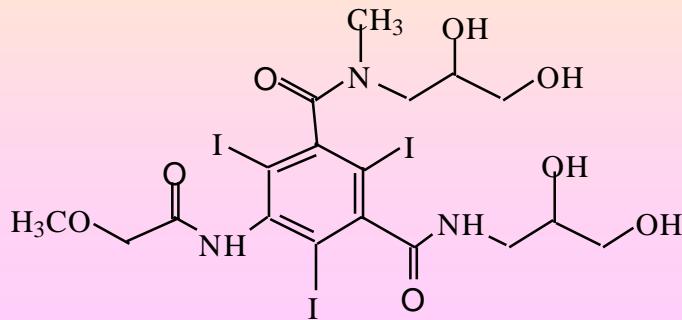
lothalamic acid



Diatrizoate

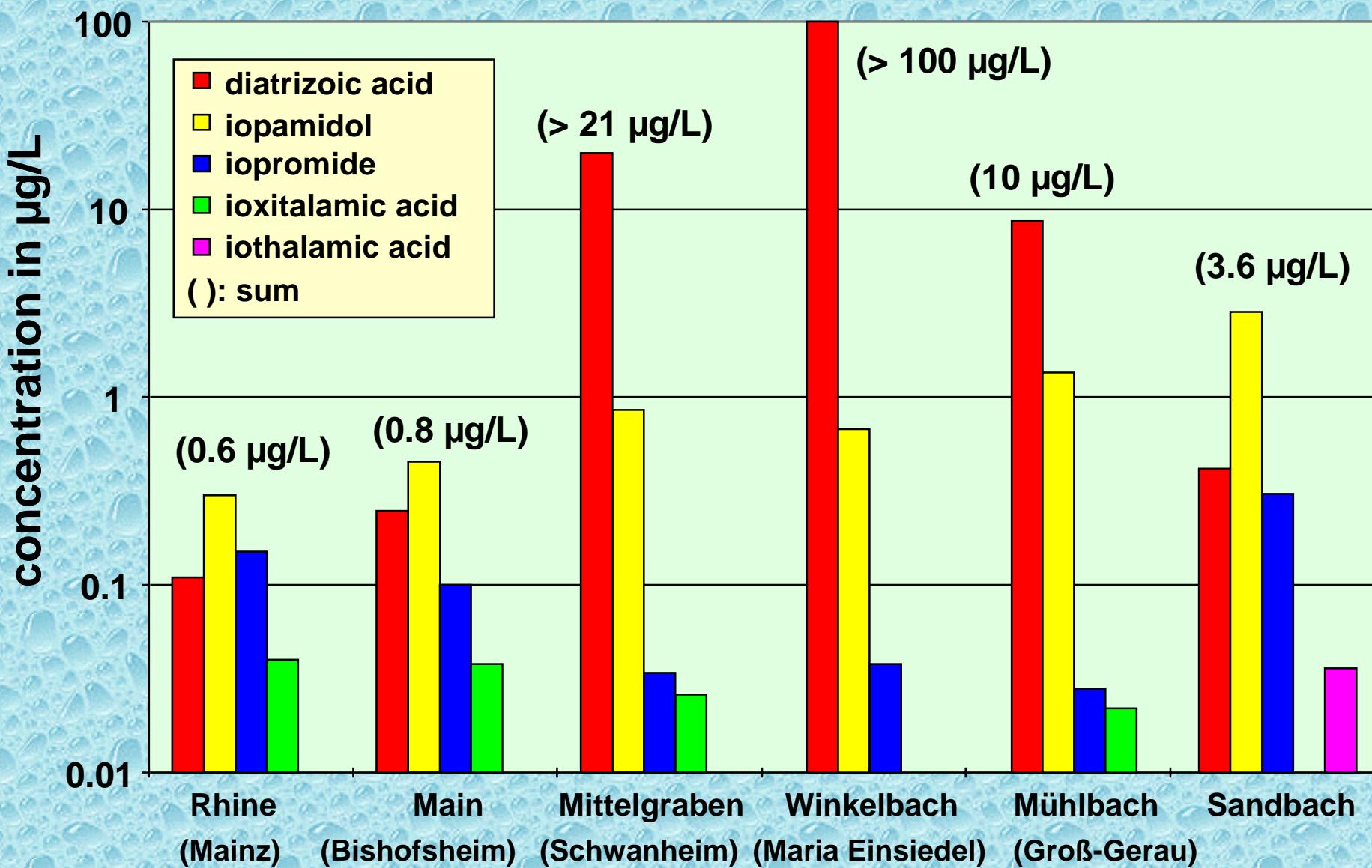


Iopamidol

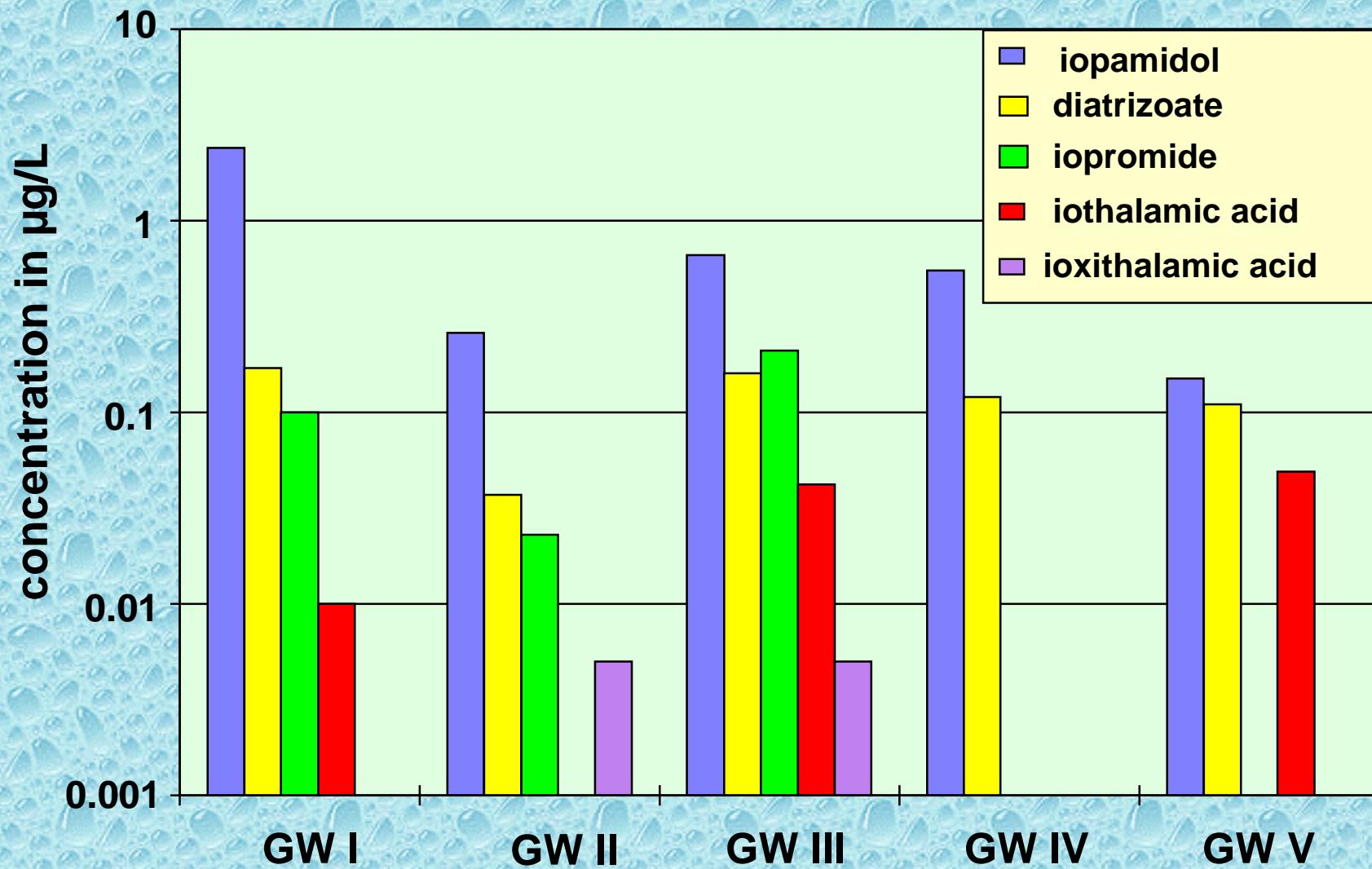


Iopromide

Iodinated contrast media in rivers and creeks

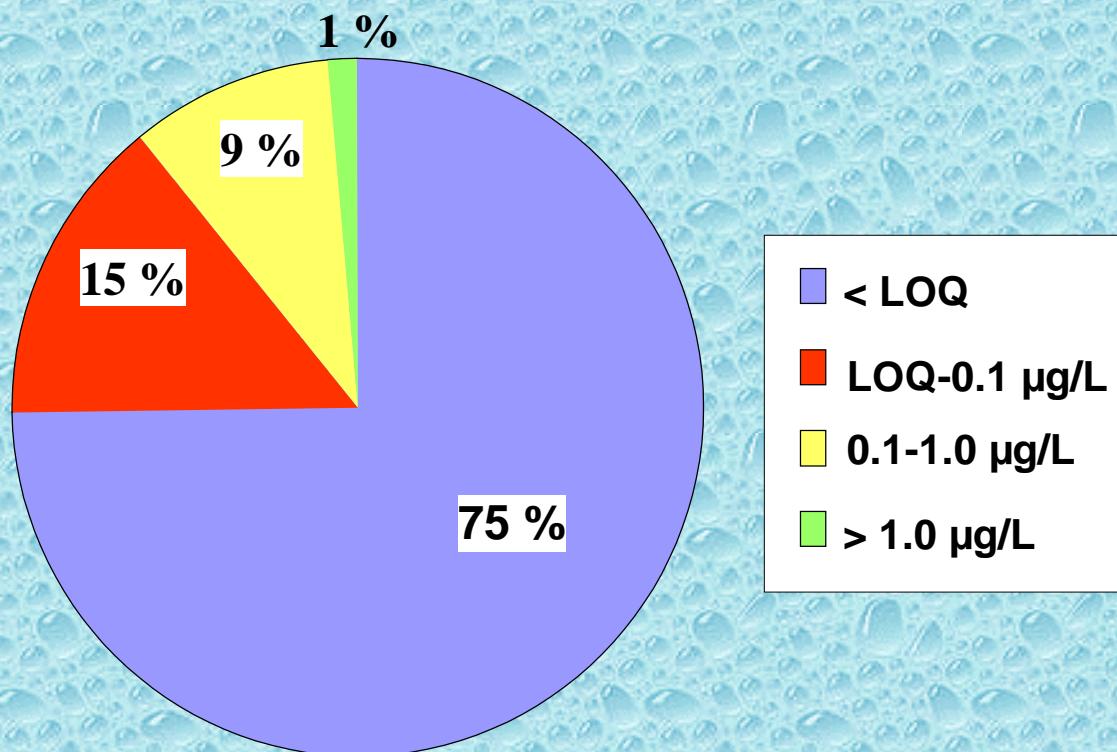


Iodinated contrast media in groundwater

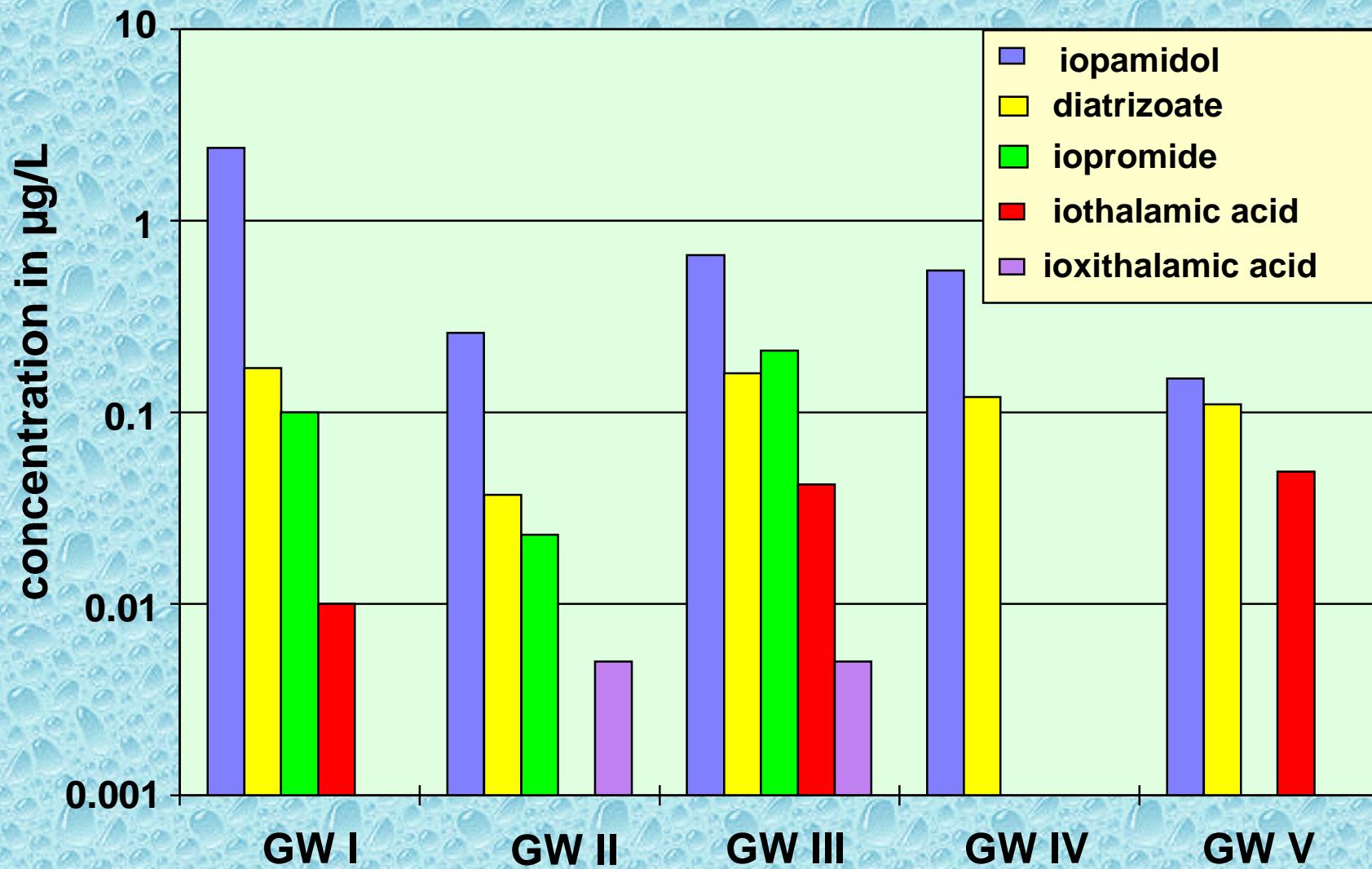


Groundwater contamination by pharmaceuticals (n=233)

	n > LOQ	maximum [µg/L]
carbamazepine	22	1.1
clofibrlic acid	79	11
diclofenac	30	0.93
bezafibrate	25	0.19



Iodinated contrast media in groundwater



Selected pharmaceuticals in German drinking waters

Substances	LOQ in µg/L	Number samples > LOQ	Number samples > 0.010 µg/L	Median in µg/L	90-Percentile in µg/L	Maximum in µg/L
Clofibrate acid	0.001	16 of 30	6	0.001	0.024	0.070
Ibuprofen	0.001	3 of 30	0	<LOQ	0.001	0.003
Diclofenac	0.001	8 of 30	0	<LOQ	0.002	0.006
Fenofibric acid	0.005	1 of 30	1	<LOQ	<LOQ	0.042
Bezafibrate	0.025	1 of 30	1	<LOQ	<LOQ	0.027
Phenazon	0.010	1 of 12	1	<LOQ	<LOQ	0.050
Carbamazepine	0.010	1 of 12	1	<LOQ	<LOQ	0.030
Iopamidol	0.010	4 of 10	4	<LOQ	0.070	0.079
Diatrizoate	0.010	5 of 10	5	0.021	0.075	0.085
Iopromide	0.010	1 of 10	1	<LOQ	<LOQ	0.086

Therapeutic Effects through Drinking Water ?

	<u>Therapy</u> <u>Minimal daily dose (DD_{th})</u> mg/d	<u>Drinking water</u> <u>Maximal daily dose (DD_{DW})</u> μg/d	<u>Safety factor</u> (DD _{th} / DD _{DW})
Diatrizoat	ca. 30000	0.27	$1,1 \times 10^8$
Clofibrac acid	250	0.81	$1,1 \times 10^5$
Bezafibrate	200	0.08	$1,1 \times 10^6$
Diclofenac	25	0.02	$1,1 \times 10^6$
Ibuprofen	200	0.01	$1,1 \times 10^7$
Fenofibric acid	100	0.13	$1,1 \times 10^6$
Carbamazepine	200	0.09	$1,1 \times 10^6$
17α-Ethinylestradiol	0.020	0.0015	$1,1 \times 10^4$

Fate of Pharmaceuticals in the Environment

Human Drugs

excretion

sewage

STP

river, creek

disposal

waste

landfill site

Drinking water

Veterinary Drugs Feed Additives

excretion

manure

soil

groundwater

(leakages)

(run-off)

Summary

Pharmaceuticals and Metabolites are ubiquitously spread in der aquatic environment

- Glucuronide conjugates can be cleaved
- Routes: STPs, landfill sites, sewer drains, irrigation
- Stability in rivers, lakes?

rivers, creeks	number analytes	> 0,01 µg/L	> 0,1 µg/L	> 1 µg/L
<i>Pharmaceuticals</i>	56	34 (61%)	25 (45%)	7 (12%)
<i>Metabolites</i>	8	7 (88 %)	6 (75%)	2 (25%)

Conceivable approaches to reduce drug residues in the aquatic environment

- ◆ Consideration of environmental risk
Assessment within the approval procedure
of drugs by the government
- ◆ Old drugs: *substitution of polluting drugs*
with environmentally compatible compounds
- ◆ Integration of *feed additives* within the
the *pharmaceutical law*
- ◆ Optimizing of the *removal efficiency*
for drugs by sewage treatment plants

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